Amendment of the Claims

Claims 3, 9, 14, 15, and 17 are amended.

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Original) A method of treating malignancies, pre-malignant conditions, and pathologic conditions in a subject which are characterized by the expression of single-chain (zymogen) and/or two-chain (activated) form of matriptase comprising administering a therapeutically effective amount of a matriptase modulating agent.

2. (Original) The method of Claim 1, wherein the malignancy and pre-malignant condition is a condition of the breast.

3. (Currently amended) The method of Claim 1, wherein the pre-malignant lesion is selected from the group consisting of atypical ductal hyperplasia of the breast, actinic keratosis (AK), leukoplakia, Barrett's ~~epiethlium~~ epithelium (columnar metaplasia) of the esophagus, ulcerative colitis, adenomatous colorectal polyps, erythroplasia of Queyrat, Bowen's disease, bowenoid papulosis, vulvar intraepithelial neoplasia (VIN), and displastic changes to the cervix.

4. (Original) The method of Claim 1, wherein the matriptase inhibiting agent is Bowman-Birk inhibitor (BBI) or a structurally related molecule or fragments thereof.

5. (Original) The method of Claim 4, wherein BBI is a BBI concentrate (BBIC).

6. (Original) The method of Claim 5, wherein the tumor formation-inhibiting effective amount of BBIC is sufficient to obtain a blood level of 0.001 to 1 mM of BBIC in the blood.

7. (Original) The method of Claim 1, wherein the biological sample is obtained by biopsy, nipple aspirate, or removal of body fluid that has come into contact with a malignant cell, cells of a pre-malignant lesion, or cells associated with a pathologic condition.

8. (Original) The method of Claim 1, wherein the malignancy, pre-malignant condition, or other pathologic condition, is in epithelial tissue or in a matriptase expressing tissue.

9. (Currently amended) A nucleic acid comprising SEQ ID NO: [[1]] 4 or SEQ ID NO: [[2]] 26.

10. (Original) A vector comprising a nucleic acid of Claim 9.

11. (Original) A cell transformed with the nucleic acid of Claim 9.

12. (Original) A method of making a recombinant matriptase comprising the steps of:

(A) transforming or transfecting a cell with a nucleic acid of Claim 9;

(B) culturing the cell under conditions in which matriptase is synthesized; and

(C) isolating matriptase from the cell.

13. (Original) A protein encoded by the nucleic acid of Claim 9.

14. (Currently Amended) A protein comprising SEQ ID NO: [[3]] 5 or SEQ ID NO: [[4]] 27 or a polypeptide fragment thereof.

15. (Currently amended) An antibody or immunogenic fragment thereof which recognizes and binds to SEQ ID NO: [[3]] 5 or a fragment thereof or SEQ ID NO: [[4]] 27 or a fragment thereof.

16. (Original) An antibody or immunogenic fragment which selectively binds to the single-chain (zymogen) form of matriptase or two-chain (active) form of matriptase.

17. (Currently amended) The antibody or immunogenic fragment thereof of Claim 14, wherein the antibody or immunogenic fragment recognizes and binds to an epitope on matriptase which comprises a domain located in amino acids 481-683 of SEQ ID NO: [[3]] 5 or SEQ ID NO: [[4]] 27, or as a region in the transmembrane domain.

18. (Original) The antibody of Claim 14, wherein the antibody is a monoclonal antibody.

19. (Original) The antibody or immunogenic fragment thereof of Claim 14, wherein the immunogenic fragment is selected from the group consisting of scFv, Fab, Fab', and $F(ab')_2$.

20. (Original) A method of inhibiting tumor invasion or tumor metastasis by administering an agent which inhibits the activation of the zymogen form of matriptase or the activity of the two-chain (active) form of matriptase expressed by a tumor cell.

21. (Original) The method of Claim 18, wherein the agent is BBIC or a structurally related inhibitor.

22. (Original) A method of identifying a compound that specifically binds to an a single-chain or a two-chain form of matriptase comprising the steps of:

(A) exposing a single-chain or two-chain form of matriptase to a compound;

(B) determining whether the single-chain or the two-chain form of matriptase specifically binds to the compound; and

(C) determining whether the compound that binds to the single-chain form of matriptase inhibits activation to the two-chain form of matriptase, or whether the compound binds to the two-chain form of matriptase and inhibits its catalytic activity.

23. (Original) An *in vitro* method of diagnosing the presence of a pre-malignant lesion, a malignancy or other pathologic condition in a subject comprising the steps of:

(A) administering to a subject, that is to be tested for a pre-malignant or malignant lesion, or other pathologic condition, which is characterized by the presence of a single-chain form of matriptase or a two-chain form of matriptase, a labeled agent which recognizes and binds either the single-chain form or the two-chain form of matriptase; and

(B) imaging the subject for the localization of the labeled agent.

24. (Original) The method of Claim 23, wherein the labeled agent is an antibody.

25. (Original) The method of Claim 24, wherein the labeled antibody is a labeled monoclonal antibody.

26. (Original) The method of Claim 23, wherein the agent is labeled with a radiolabel or a fluorescent label.

27. (Original) The method of Claim 26, wherein the radiolabel is selected from the group consisting of: ^{62}Cu, ^{99}Te, ^{131}I, ^{123}I, ^{111}In, ^{90}Y, ^{188}Re, and ^{186}Re.

28. (Original) An *in vitro* method of diagnosing the presence of a pre-malignant lesion, a malignancy, or other pathologic condition, in a subject, which is characterized by the presence of a single-chain form and/or a two-chain form of matriptase comprising the steps of:

(A) obtaining a biological sample from a subject that is to be tested for a pre-malignant lesion, a malignancy, or other pathologic condition;

(B) exposing the biological sample to a labeled agent which recognizes and binds to the single-chain or two-chain form of matriptase; and

(C) determining whether said labeled agent bound to the biological sample.

29. (Original) The method of Claim 27, wherein the biological sample is a sample comprising epithelial cells.

30. (Original) The method of Claim 27, wherein the labeled agent is a labeled antibody.

31. (Original) The method of Claim 30, wherein the labeled antibody is labeled with a radioisotope or a fluorescent label.

32. (Original) The method of Claim 31, wherein the radioisotope is selected from the group consisting of: ^{62}Cu, ^{99}Te, ^{131}I, ^{123}I, ^{111}In, ^{90}Y, ^{188}Re, and ^{186}Re.

33. (Original) A method of identifying a compound that specifically binds to a single-chain or a two-chain form of matriptase comprising the steps of:

(A) identifying by molecular modeling a compound that putatively binds to the activation site on the single-chain form of matriptase, the catalytic site of the two-chain form of matriptase, the Clr/Cls domain of either form of matriptase, or other regulatory domain;

(B) contacting said compound with said single-chain form or two-chain form of matriptase;

(C) determining whether said compound binds to the single-chain form or the two-chain form of matriptase; and

(D) if the compound binds to a form of matriptase, further determining whether the compound exhibits at least one of the following properties: (i) inhibits activation of the single-chain form of matriptase to a two-chain form of matriptase, (ii) binds to the two-chain form of matriptase and thereby inhibits its catalytic activity, and (iii) binds to the C1r/Cls domain or other regulating domain, and thereby inhibits dimerization of the protein.